GW25-e3226

Influence of Exhaustive Exercise on HR and Brain Functional Connectivity with fMRI Research

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Objectives: Many theories regarding the mechanisms underlying exercise-induced fatigue have focused on changes within the muscle. Such as run-down of the high energy reserves of the cell, an accumulation of lactate, H+ and free radical content. Central fatigue was first defined as the condition in which "during a sustained fatiguing contraction, voluntary activation declines progressively". The aim of this study was to examine nucleons functional connectivity in resting state after exhaustive cycle ergometer exercise. Furthermore, we investigated whether the CNS executive function is influenced.
Methods: Eleven healthy, right-handed and right leg dominant subjects participated in this study after signing an informed consent. Participants completed the exhaustive exercise protocols on a cycle ergo meter. Heart rate was measured every 5s using short-range radio telemetry (S725XPolar, Finland). Participants completed a five-minute warm-up at a cadence of 50revmin-1, 50W, 100W for the second stage, to 150W for the third stage and 200W for the final stage. The state of exhaustive exercise is when the participant cannot maintain the cadence and the heart rate arrived above 90% of the maximum heart rate. The MR protocol was carried out at 3T with fMRI. Functional images were preprocessed using SPM5 software.
Results: At the conclusion of exhaustive exercise the participant heart rate is above 90% of the maximum HR (67±7.38 to 198±8.55). Blood lactate concentration is significantly increased ($P<0.01$). The motor task in this experiment caused statistical significant positive activities in these brain areas for both before and after: sensor motor area, premotor area, supplementary motor area, cerebellum, and basal ganglia. Lateral frontal area and some temporal areas were significantly activated only before exhaustive exercise state.
Conclusions: Human brain activity during a resting-state has attracted increasing attention. Brain consists of different brain regions that each has their own specific task and function. They form a large and complex network, which sharing information with each other. Functional connectivity is defined as the temporal dependence of neuronal activity patterns of anatomically separated brain regions. The activation of thalamus and basal ganglia area were significantly decreased, as well as the cluster sizes of this two activation areas. To be contrast, SMA, cerebellum, insula and hippocampus areas were less active after exhaustive exercise.

GW25-e3283

fMRI Research of Response Inhibition in High-level Soccer Players

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Objectives: Response inhibition refers to the suppression of actions that are inappropriate in a given context and that interfere with goal-driven behavior. In order to explore the neural mechanisms during inhibition process in motor control, we use fMRI research method together with Go\No\Go task to observe the reaction characteristics of high-level soccer players and ordinary college students.
Methods: The MR protocol was carried out with 3T whole-body system (Siemens, Erlangen, Germany) using blood oxygen level-dependent (BOLD) fMRI. All subjects underwent a comprehensive verbal screen to ensure that they did not meet any of the exclusive criteria for fMRI experimentation. Functional images were preprocessed using SPM5 software (Welcome Department of Cognitive Neurology, London, UK).
Results: The results showed that functional areas involved in inhibition process dominated by sensorimotor area, premotor area, supplementary motor area, basal ganglia, right Superior Frontal Gyrus, Middle Frontal Gyrus, Middle Temporal Gyrus, right temporal lobe, and occipital cortex in response to the success of the two groups. And active areas and of high-level soccer players were less than that of ordinary college students.
Conclusions: Response inhibition is the suppression of actions that are inappropriate in a given context and that interfere with goal-driven behavior. Stop tasks are the most common measure of response inhibition and gauge the speed and behavioral inhibitory (stopping) processes and the ability to effectively trigger inhibitory processes. Response inhibition is considered a key cognitive deficit of Schizophrenia and Attention Deficit Hyperactivity Disorder. Executive control processes and frontal sub cortical circuits are considered critical to response inhibition. Pre-SMA circuits and basal ganglia are critical to selection of appropriate behavior.

GW25-e4214

The Role of Xuebijing Injection in Modulation of Heart Rate Variability and Dynamics in the Sepsis Rats

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Objectives: Xuebijing Injection (XBJ) is separated from Chinese herbs, with satisfactory antiendotoxin and anti-inflammatory effects shown in clinical trials. This study was to assess the role of XBJ in modulation of heart rate Variability and dynamics in the sepsis rats.
Methods: Ninety adult male Sprague-Dawley rats were used (Each 30 for examination of cytokine production and electrocardiographic (ECG) recordings after CLP for 18h or 72h separately; 30 for survival analysis). Each part of the study involved 3 animal groups, including sham operated group, with or without drug administration groups (CLP group and CLP+XBJ group). Sepsis was induced by cecal ligation and puncture (CLP). XBJ injection (5 ml/kg) was administered after surgery for 6h. ECG was recorded for 5 min after surgery for 18h or 72 h separately for heart rate variability (HRV) and ECG analysis in CLP and CLP+XBJ groups. Blood samples were collected at the end of experience for serum cytokine assay.
Results: XBJ injection significantly improve CLP group 10d-survival rate (70% vs 40%), and inhibited IL-6, High-mobility group box 1 protein (HMGB1) and C5a induction in the CLP group after surgery for 18 h and 72 h respectively. Heart rate (HR) and RR interval were markedly increased in CLP group after surgery for 18 h, but did not significantly change after CLP for 72 h. On the contrary, QTc interval was obviously extended in CLP group after surgery for 72 h than in sham-operated group. XBJ injection can effectively decrease the change of HR and RR interval compared with CLP group (HR: 437±16 vs 460±12; RR interval: 0.137±0.005 vs 0.130±0.003), but has no effect on the change of the QT interval. HRV analysis demonstrated a significant increase in the ratio of low-frequency power (LF) / high-frequency power (HF) and LF/ (LF+HF) in the CLP animals compared with the sham-operated group after surgery for 18 h, but decrease the ratio of LF/HF and LF/ (LF+HF) after surgery for 72 h. XBJ injection significantly regulate the change of HRV index [LF/ (LF+HF) in 18 h: 0.570±0.087 vs 0.377±0.124; LF/ (LF+HF) in 72 h: 0.562±0.117 vs 0.398±0.140].
Conclusions: CLP-induced sepsis could show bidirectional regulatory affection in HRV, and sympathetic overstimulation and further excessive inhibition could appear with the development of sepsis. XBJ injection can obviously control excess cytokine production and sympathetic change in the pathogenesis of severe sepsis and increases the survival rate.

GW25-e5133

Phosphatase and tensin homologue on chromosome 10 regulates angiotensin II-induced proliferation and collagen metabolism in neonatal rat cardiac fibroblasts through the Akt/P27 signaling pathway

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Objectives: Cardiac fibroblasts (CFs) play a key role in cardiac fibrosis by regulating the balance between extracellular matrix production and breakdown. Phosphatase and tensin homologue (PTEN) on chromosome 10 has been found to play an important role in cardiovascular disease, but it is not clear whether PTEN is involved in functional regulation of CFs. To observe whether PTEN is involved in functional regulation of CFs, and how it works.
Methods: PTEN was overexpressed in neonatal rat CFs by gene transfer of recombinant adenovirus. Then, we investigated whether PTEN plays an important role in Angiotensin (Ang) II-induced CF proliferation, apoptosis, the cell cycle, and collagen metabolism as well as the possible molecular mechanisms.
Results: Compared with the untreated and green fluorescent protein-expressing adenovirus (Ad-GFP) groups, PTEN adenovirus (Ad-PTEN) infection increased PTEN protein and mRNA expression in CFs. Ad-PTEN increased the proportion of CFs in G1/S phase events with no change in cell apoptosis. In addition, Ad-PTEN decreased mRNA expression and the protein synthesis rate of collagen type I and III, and antagonized Ang II-induced collagen synthesis. Overexpression of PTEN also decreased Ang II-induced matrix metalloproteinase-2 (MMP-2) and tissue inhibitor of metalloproteinase-1 (TIMP-1) production as well as gelatinase activity. Moreover, Ad-PTEN decreased Akt expression and increased P27 expression with or without Ang II stimulation.
Conclusions: These results suggested that PTEN could regulate Ang II-induced collagen metabolism in neonatal rat CFs through the Akt/P27 signaling pathway, thus providing a new possible target for the treatment of cardiac fibrosis.

GW25-e5153

Effect of Hirulog-like peptide on middle cerebral artery occlusion-induced brain injury in mice

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Objectives: Hirulog-like-peptide, similar to the low-molecular-weight heparin is a thrombin inhibitor. Our previous study demonstrated that hirulog-like-peptide could reduce vascular neointimal formation or restenosis in animals undergoing balloon catheter injury in carotid artery. However, the function of hirulog-like-peptide during ischemic stroke is largely unknown. Here, weinvestigate the effect of hirulog-like-peptide on brain injury, which was induced by suture middle cerebral artery occlusion in mice.
Methods: Ischemic stroke was induced by transient suture insertion into the opening of middle cerebral artery for 90 minutes. Mice were treated with hirulog-like-peptide and

low-molecular-weight heparin or saline were serve as the controls. Infarct volume, neurologic deficits and apoptotic factors were measuredfollowing1 to 14 days of ischemia.
Results: We demonstrated that hirulog-like-peptide intravenous injection alleviated brain infarct volume and improved neurologic outcomes (P<0.05). Hirulog-like-peptidecould attenuate the levels of PAR-1, caspase-3, malondialdehyde and Bax, increase of catalase and Bcl-2 activity, and could also improve the ratio of Bcl-2 / Bax compared to the controls (P<0.05).
Conclusions: Hirulog-like-peptide treatment following ischemic stroke attenuated infarct volume, improved the neurologic outcomes. Hirulog-like-peptide treatment had stronger beneficial effects on the regulation of thrombin receptor and key apoptosis regulators in the mouse brain, suggesting hirulog-like-peptide treatment is a potential alternative in stroke therapy.

GW25-e0301

Effect of the imbalance between matrix metalloproteinase-9 and tissue Inhibitor of metalloproteinase-1 on cardiac function after cardiopulmonary resuscitation

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Objectives: To determine (a) there was an imbalance between matrix metalloproteinase-9 (MMP-9) and tissue inhibitor of metalloproteinase-1 (TIMP-1) after CPR in a canine model of prolonged ventricular fibrillation (VF) ; (b) with the duration of VF, the degree of the imbalance would be greater; and (c) whether there was a relationship between the level of MMP-9 or TIMP-1 and the cardiac function.
Methods: VF was electrically induced in 24 dogs. The animals were randomly divided into three groups (sham control: n=8; 8-min VF: n=8; 12-min VF: n=8). Echocardiographic measurement and hemodynamic variables were recorded before VF and after return of spontaneous circulation (ROSC). TIMP-1 and MMP-9 were analyzed by Western blot and immune histochemistry.
Results: After ROSC, the hemodynamic variables decreased, the dimensions of the left atrium (LAD) and left ventricular diastolic (LVDd) enlarged and the left ventricular ejection fraction (LVEF) declined in each VF group (P<0.05). Compared with 8-min VF group, the LAD was much larger and the LVEF was much lower in 12-min VF group (P<0.05). Compared with sham controls, dogs under VF and CPR showed significantly decreased level of TIMP-1 (P<0.05), and with the duration of VF, the level of TIMP-1 declined (P<0.05). The level of MMP-9 did not achieve statistical significance in the three groups (P>0.05), however, they were higher in VF and longer-duration VF groups. The ratios of TIMP-1/MMP-9 were lower in VF groups (P<0.05). There was a negative correlation between TIMP-1 and the LAD and LVDd (r=-0.83, r=-0.96, respectively, P<0.05), and a positive correlation between TIMP-1 and the LVEF (r=0.85, P<0.05).
Conclusions: There was an imbalance between TIMP-1 and MMP-9 after CPR. It may partly contribute to the post-resuscitation cardiac dysfunction.

GW25-e0609

Renalase gene polymorphism in patients with hypertension and concomitant coronary heart disease

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Objectives: This study aimed to investigate renalase gene polymorphism in patients with hypertension and concomitant coronary heart disease (CHD) and to evaluate the risk for CHD in hypertensive patients from the view of genetics.
Methods: NCBI and HapMap genome database were employed to screen the Single nucleotide polymorphisms (SNP). These SNPs were detected in hypertensive and CHD patients (n=791), hypertensive patients (n=802) and healthy controls (n=812), and the genotypes were recorded. Haploview 4.2 software was used to determine the genotypes, allele frequency, haplotypes, linkage disequilibrium and Hardy-Weinberg (HWE) equilibrium, and odds ratio (OR) was calculated with non-conditioned logistic regression analysis.
Results: The frequency of allele A of rs2576178 in patients with hypertensive and CHD was markedly higher than that in hypertensive patients (P=0.001, OR=1.625, 95% CI 1.221-2.160). The frequency of allele C of rs2296545 in hypertensive patients was significantly higher than that in healthy controls (P=0.009, OR=1.436, 95% CI 1.095-1.883).
Conclusions: The allele A of rs2576178 may be a predisposing factor of CHD in hypertensive patients, and hypertensive patients with AA genotype are susceptible to develop CHD. The allele C of rs2296545 may be a predisposing factor of hypertension and patients with CC genotype are susceptible to develop hypertension.

GW25-e0299

Zp123 Reduces Defibrillation Energy by Preventing Connexion-43 Remodeling in Prolonged Ventricular Fibrillation in Swine

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Objectives: To study the effect of Zp123 on defibrillation energy requirements during ventricular fibrillation (VF) using an in vivo pig model system.
Methods: Thirty-three pigs were employed in data analysis; one pig in the control group was excluded due to death during catheterization. Zp123 treatment did not alter ECG variables. The average defibrillation energy required in the Zp123 group was lower than that in the control group (327.28±269.60J vs. 610.00±192.64J P=0.015). The cumulative percentage of successful defibrillation at every energy level in the Zp123 group was higher than that in the control group (P<0.05). Additionally, pigs in the Zp123 group were more often in supraventricular rhythm than those in the control group (72.7% vs. 50.0%, P< 0.05). Results obtained using both of western blots and immunofluorescence showed that Zp123 did not alter the total amount of Connexion-43 but prevented its dephosphorylation.
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Conclusions: Zp123 can reduce defibrillation energy requirements by preventing Connexion-43 remodeling during prolonged VF.

GW25-e0597

Investigation of the mechanism underlying the antihypertensive effect of catheter-based radiofrequency renal sympathetic denervation on hypertension in hypertensive dogs

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Objectives: This study aimed to assess the antihypertensive efficacy and safety of catheter-based radiofrequency renal sympathetic denervation (RSD) in hypertensive dogs. Furthermore, this study attempted to investigate the possible antihypertensive mechanism of radiofrequency RSD through measuring the postoperative serum concentrations of angiotensin II (AngII), NADPH oxidase (NADPH-ox), malondialdehyde (MDA), nitric oxide (NO), and endothelial nitric-oxide synthase (eNOS) following radiofrequency RSD.
Methods: A total of 12 beagles were randomly divided into the operation group (n=6) and the sham-operation group (n=6). The hypertension model was established using ahigh-fat diet. The operation group received catheter-based radiofrequency RSD, while the sham-operation group only received renal arteriography. Blood pressure was measured prior to the operation and 3 days, 1 week, 2 weeks, 1 month, 2 months, and 3 months after the operation. The serum concentrations of AngII, NADPH-ox, MDA, NO, and eNOS were measured prior to the operation and 1 week, 1 month, and 3 months after the operation.
Results: (1) After the model was established, the systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and mean arterial pressure (MAP) of the operation group and the sham-operation group were all significantly increased above baseline (P<0.05), but there was no significant difference between the two groups. (2) SAP, DAP, and MAP in the operation group at 1 and 3 months after the operation were significantly decreased compared to the levels measured prior to the operation and those in the sham-operation group (P<0.05). Three months after the operation, the serum creatinine level was normal, and renal arteriography did not show renal artery stenosis. (3) Compared to those measured prior to the operation, the concentrations of serum AngII, NADPH-ox, and MDA in the operation group at 1 week, 1 month, and 3 months after the operation were decreased, while the concentrations of serum NO and eNOS were increased (P<0.05). The above indicators measured at the same time points demonstrated statistically significant differences between the operation group and the sham-operation group (P<0.05).
Conclusions: Catheter-based radiofrequency RSD may inhibit the renin-angiotensin system (RAS) and the oxidative stress response as well as improve vascular endothelial function, thus significantly reducing blood pressure through the reduction of sympathetic activity in hypertensive dogs.

GW25-e0717

Lycopene protects cardiomyocytes from hypoxia/reoxygenation injury via attenuating endoplasmic reticulum stress

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Objectives: The present study was designed to investigate whether lycopene could efficiently protect cardiomyocytes from H/R-injury via attenuating ER stress.
Methods: Primary cardiomyocytes were isolated from neonatal C57 mice and divided into four groups: control, lycopene, H/R, lycopene+H/R. After cultured for 48 to 72 hours, cardiomyocytes were exposed to H/R-treatment to investigate the underlying protective mechanism of lycopene on H/R-injury. Cell viability was estimated by CCK-8 kits and cell apoptosis was detected by TUNEL labeling staining. The activity of caspase-3 was determined using the caspase-3 Activity Assay kit. Expressions of GRP78 and CHOP were estimated by western blot.